REMARKS

Claims 1-11 are pending in the present Application. Claims 4 and 9 are canceled without prejudice and new claim 12 is added, thus leaving Claims 1 - 3, 5 – 8, and 10 –12 for consideration upon entry of the present Amendment. Claims 1, 2 and 10 are amended. Support for the amendments to claims 1, 2 and 10 is found at least at p. 4, lines 32-33 and examples 4 and 5; support for new claim 12 is found at least in claim 1 as filed and in examples 4 and 5. No new matter has been introduced by these amendments.

Reconsideration and allowance of the claims are respectfully requested in view of the above amendments and the following remarks.

Claim Objections

Claims 1, 2, 9 and 10 stand objected to for informalities. (Office Action dated 11/23/2005, page 2) Specifically, with regard to Claim 1, the Examiner stated that the element "performed in the absence of an additional probe to . . ." is unclear. Applicants have clarified Claim 1 by amending the element to "performed in the absence of a probe to . . .".

With regard to Claim 2, the Examiner stated that the element "wherein the electrode does not . . .", is unclear in that there is not a single electrode in Claim 1. Applicants have clarified Claim 2 as suggested.

Claims 9 and 10 stand objected to for not containing proper grammatical flow. Applicants assert that in view of current amendments to claims 1 and 10 and cancellation of claim 9, this objection is moot.

Applicants respectfully request a withdrawal of the objections to claims 1, 2 and 10.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 1-11 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over U.S. Patent No. 6,264,825 to Blackburn et al. (hereinafter Blackburn) in view of U.S. Patent No. 6,169,394 to Frazier et al. (hereinafter Frazier). (Office Action dated 11/23/2005, page 3) Applicants respectfully traverse this rejection.

For an obviousness rejection to be proper, the Examiner must meet the burden of establishing a *prima facie* case of obviousness, i.e., that all elements of the invention are disclosed

in the prior art; that the prior art relied upon, coupled with knowledge generally available in the art at the time of the invention, contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or combined references; and that the proposed modification of the prior art had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988); *In Re Wilson*, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970); *Amgen v. Chugai Pharmaceuticals Co.*, 927 U.S.P.Q.2d, 1016, 1023 (Fed. Cir. 1996).

Blackburn generally discloses compositions and methods useful in the acceleration of binding of target analytes to capture ligands on surfaces. Detection proceeds through the use of an electron transfer moiety (ETM) that is associated with the target analyte, either directly or indirectly, to allow detection of the ETM. (Abstract)

Frazier generally discloses a micro-electric detector for conductivity or impedance-based measurements of a test sample placed in a microchannel of a micro-analysis system. (Abstract)

As amended, Claim 1 discloses a method for detecting a polymerase chain reaction (PCR) product, comprising: providing at least a pair of electrodes in a PCR solution-containing vessel, wherein the pair of electrodes is connected to an impedance sensor; performing PCR; producing an electric field between the pair of electrodes; and measuring a change in impedance magnitude of the PCR solution after a PCR cycle, wherein the measuring is performed in the absence of a probe for generating an electrical signal.

Applicants can find no statements in either Blackburn or Frazier that teach or suggest all the elements of the claimed invention. Specifically, neither Blackburn, nor Frazier teach or suggest a method in which a PCR product could be detected during a PCR reaction by measuring the impedance magnitude of the PCR solution after a PCR cycle, wherein the measuring is performed in the absence of a probe for generating an electrical signal.

The method of Blackburn et al. uses a detection electrode comprising a covalently attached capture ligand (Blackburn et al. col. 2, lines 15-18) or a self-assembled monolayer with a capture ligand (col. 2, lines 61-63). Detection of a target analyte proceeds through the use of an electron transfer moiety (ETM) that is associated with the target analyte, either directly or indirectly, to allow detection of the ETM (Abstract).

Frazier discloses a micro-electric impedance detector, however Applicants can find no

teaching or suggestion in Frazier of measuring a change in impedance magnitude of a PCR solution after a PCR cycle, wherein the measuring is performed in the absence of a probe for generating an electrical signal. Frazier teach use of their detector for detecting particulate-containing fluids and biological materials, such as living cells or subcellular structures, and for noninvasive interrogation of cellular materials (Column 13, lines 8-32). Thus, neither Blackburn nor Frazier teach or suggest all elements of claim 1.

Further, even assuming that all elements of an invention are disclosed in the prior art, an Examiner cannot establish obviousness by locating references that describe various aspects of a patent applicant's invention without also providing evidence of the motivating force which would have impelled one skilled in the art to do what the patent applicant has done. *Ex parte Levengood*, 28 U.S.P.Q.2d 1300 (Bd. Pat. App. Int. 1993). The references, when viewed by themselves and not in retrospect, must suggest the invention. *In Re Skoll*, 187 U.S.P.Q. 481 (C.C.P.A. 1975). Also, the requirement for a determination of obviousness is that "both the suggestion and the expectation of success must be founded in the prior art, not in applicant's disclosure" (emphasis added). *In re Dow Chem.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). In applying Section 103, the U.S. Court of Appeals for the Federal Circuit has consistently held that one must consider both the invention and the prior art "as a whole", not from improper hindsight gained from consideration of the claimed invention. See, *Interconnect Planning Corp. v. Feil*, 227 U.S.P.Q. 543, 551 (Fed. Cir. 1985) and cases cited therein.

Applicants assert that the Examiner has failed to establish that the requisite motivating force to combine Blackburn with Frazier and the requisite expectation of success were present in the cited references, particularly when the references are considered "as a whole".

Blackburn teaches that "One of the significant hurdles in biosensor applications is the rate at which the target analyte binds to the surface for detection and the affinity for the surface" (col. 1, lines 53-55). Blackburn addresses that hurdle by teaching compositions and methods useful for accelerating binding of target analyte to surfaces. Applicants can find no teaching or suggestion in Blackburn for detecting target analytes (for example a PCR product) without use of one or more of the compositions disclosed by Blackburn.

Applicants can find no teaching or suggestion in Frazier to use their micro-electric detector in measuring a change in impedance magnitude of a PCR reaction, either in the presence of

Blackburn's compositions or, as required by claim 1, in the absence of such compositions (a probe for generating the electrical signal). The Examiner states in the Office Action, at p. 4, 2nd paragraph, that Frazier discusses detection of PCR systems, however there is no indication of where in Frazier this discussion occurs. Applicants can find no such discussion in Frazier. In the Background section of Frazier, although there is mention that PCR is one type of biological or chemical analysis technique that has been demonstrated in a micro-scale system and implemented using micromachining technology (col. 2, lines 48-56), Applicants can find no teaching or suggestion in Frazier that the device of Frazier is suitable for detection of a PCR product. Rather, Frazier teaches that the disclosed micro-electric detector is suited to monitor particulate containing fluids, such as fluids containing biological materials including living cells and subcellular structures. (Column 4, lines 26 - 31) Nor does Frazier teach or suggest that a PCR product could be detected electrically without having the PCR product bound to a capture ligand forming an assay complex comprising at least one electron transfer moiety.

Further, in view of Blackburn's strong arguments for the need for their compositions and methods to detect a target analyte such as a PCR product and the lack of any teaching in Frazier that a PCR product could be detected electrically without having the PCR product bound to a capture ligand forming an assay complex comprising at least one electron transfer moiety, if a skilled person were motivated by the teachings of Blackburn and Frazier to combine the two, the result would be a combination in which Frazier's detection device was used with the compositions and methods of Blackburn, not in the method of claim 1. Thus, the prior art relied upon does not contain any language that would have motivated one of ordinary skill in the art to combine the method of Blackburn with the detection system of Frazier.

Additionally, in view of Blackburn's strong arguments for the need for their compositions and methods to detect a target analyte such as a PCR product and the silence of Frazier with respect to use of their device in detection of a PCR product or success in detecting a PCR product without binding the product to a capture ligand to form an assay complex comprising at least one electron transfer moiety, Applicants assert that a skilled person would not have any expectation of success in using Frazier's detection device in a method disclosed by Blackburn, without the presence of a composition of Blackburn (a probe for generating the electrical signal).

Thus, Applicants assert that the Examiner has failed to establish the *prima facie*

obviousness of claim 1 over Blackburn in view of Frazier because the combination of references do not teach or suggest all elements of claim 1 and because the combination of references, when taken as a whole, would not provide a skilled practitioner with motivation to combine the two references to obtain claim 1 or with any expectation that the combination, lacking Blackburn's compositions, would have any success. Applicants therefore request reconsideration and withdrawal of the rejection of Claim 1 under U.S.C. § 103.

Claims 2 - 3, 5 – 8, and 10-11 depend from Claim 1 and must include all the limitations of the base claim. Accordingly, a *prima facie* case of obviousness of Claims 2 – 3, 5 – 8, and 10-11 has not been successfully made, due to their dependency on Claim 1. Applicants therefore request reconsideration and withdrawal of the rejection of Claims 2 – 3, 5 – 8, and 10 - 11 under U.S.C. § 103 and an allowance of the claims in view of the above amendments and remarks.

Allowable subject matter

Claims 10 and 11 stand objected to as being dependent upon a rejected base claim, but allowable if rewritten to include all limitations of the base and any intervening claims (Office Action dated 11/23/2005, page 5). Applicants thank the Examiner for noting that claims 10 and 11 are directed to allowable subject matter. Claims 10 and 11 ultimately depend from Claim 1. As Applicants believe that the foregoing amendments and remarks place Claim 1 in condition for allowance, Applicants have not rewritten claim 10 as an independent claim.

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Conclusion

It is believed that the foregoing amendments and remarks fully comply with the Office Action and that the claims herein should now be allowable to Applicants. Accordingly, reconsideration and allowance are requested.

If there are any additional charges with respect to this Amendment or otherwise, please charge them to Deposit Account No. 06-1130.

Respectfully submitted,

CANTOR COLBURN LLP

By: _____
Sandra L. Shaner
Reg. No.: 47,934

Date: February 22, 2006
CANTOR COLBURN LLP
55 Griffin Road South
Bloomfield, CT 06002
Telephone (860) 286-2929
Facsimile (860) 286-0115
PTO Customer No. 23413